

IN THE SPECIFICATION:

Please amend the paragraph on page 1, lines 7-16, as shown below:

--This application is a continuation of U.S. Application Serial No. 09/245,764, filed February 5, 1999, which claims priority under 35 U.S.C. § 119(e) from U.S. Provisional Application No. 60/073,972, filed February 6, 1998, entitled "CRYSTALS, CRYSTAL STRUCTURES OF FcγRIIa, AND USES THEREOF". ~~This application, and which~~ also claims priority under 35 U.S.C. § 119(e) from U.S. Provisional Application No. 60/099,994, filed September 11, 1998, entitled "THREE DIMENSIONAL STRUCTURES AND MODELS OF Fc RECEPTORS AND USES THEREOF." The entire disclosure of each of U.S. Application Serial No. 09/245,764, U.S. Provisional Application Nos. 60/073,972 and 60/099,994 is incorporated herein by reference.--

Please amend the paragraph bridging page 10, line 28 to page 11, line 14, as follows:

--Another embodiment of the present invention is a therapeutic composition that is capable of stimulating an IgG humoral immune response in an animal. Yet another embodiment of the present invention is a therapeutic composition that improves the therapeutic affects of an antibody that is administered to an animal to treat, by [opsinization] opsonization or FcγR-dependent effector functions (e.g. antibody-dependent FcγR-mediated cytotoxicity, phagocytosis or release of cellular mediators), a particular disease, including, but not limited to, cancer or infectious disease (e.g. oral infections such as HIV, herpes, bacterial infections, yeast infections or parasite infections). Such a therapeutic composition includes one or more stimulatory compounds that have increased binding to IgG, enhance binding of IgG to FcγR, enhance dimer formation of an FcγR and/or enhance signal transduction through the FcγR. Also included in the present invention is a method to stimulate a humoral immune response. The method includes the step of administering to an animal a therapeutic composition of the present invention.--

Please amend the paragraph bridging page 12, line 26 to page 13, line 9, as follows:

--Another embodiment of the present invention is a therapeutic composition that is capable of stimulating a IgE humoral immune response in an animal. Yet another embodiment of the present invention is a therapeutic composition that improves the therapeutic affects of an antibody that is

administered to an animal to treat, by [opsinization] opsonization or FcεR-dependent effector functions (e.g. phagocytosis or release of cellular mediators), a particular disease. Such a therapeutic composition includes one or more stimulatory compounds that have increased binding to IgE, enhance binding of IgE to FcεRI, enhance dimer formation of FcεRI and/or otherwise enhance signal transduction through the FcεRI. Also included in the present invention is a method to stimulate a humoral immune response. The method includes the step of administering to an animal a therapeutic composition of the present invention.--

On page 13, line 12, immediately following the subheading "BRIEF DESCRIPTION OF THE FIGURES", please insert the following paragraph:

--The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application with color drawing will be provided by the Office upon request and payment of the necessary fee.--

Please amend the two paragraphs bridging page 52, line 6 to page 54, line 7, as follows:

--One embodiment of the present invention is a therapeutic composition that is capable of reducing IgG-mediated tissue damage. Suitable therapeutic compositions are capable of reducing IgG-mediated tissue damage resulting from IgG-mediated hypersensitivity or other biological mechanisms involved in IgG-mediated recruitment of inflammatory cells that involves FcγR protein. For example, a therapeutic composition of the present invention can: (1) inhibit (i.e., prevent, block) binding of FcγR protein on a cell having an FcγR protein (e.g., B cells, macrophage, neutrophil, eosinophil or platelet cells) to an IgG immune complex by interfering with the IgG binding site of an FcγR protein; (2) binding to the Fc portion of IgG to inhibit complement fixation by an IgG immune complex by interfering with the complement binding site of an IgG molecule; (3) inhibit precipitation of IgG or IgG immune complexes (i.e., prevent Fc:Fc interactions between two IgG); (4) inhibit immunoglobulin-mediated cellular signal transduction by interfering with the binding of an IgG to a cell surface receptor; (5) inhibit FcγR-mediated cellular signal transduction by interfering with the binding of a cell signal inducing molecule (i.e., a molecule that induces cellular signal transduction through an FcγR protein) to an FcγR protein; (6) inhibit [opsinization] opsonization

of pathogens by inhibiting binding of IgG bound to a pathogen to FcγR protein on a phagocytic cell (e.g., to prevent antibody dependent enhancement (ADE) of viral infection, such as with flaviviruses and dengue virus); and (7) inhibit the binding of viral molecules to FcγR protein (e.g., measles virus nucleocapsid protein). As used herein, the term “immune complex” refers to a complex that is formed when an antibody binds to a soluble antigen. As used herein, the term “complement fixation” refers to complement activation by an antigen:antibody complex that results in recruitment of inflammatory cells, typically by assembly of a complex comprising C3a and C5a, or generation of cleaved C4. As used herein, the term “binding site” refers to the region of a molecule (e.g., a protein) to which another molecule specifically binds. Such therapeutic compositions include one or more inhibitory compounds that inhibit binding of IgG to FcγR protein, IgG to complement, IgG to IgG, IgG to a cell surface receptor, a cell signal inducing molecule to FcγR protein, FcγR protein to virus or inhibit [opsinization] opsonization. Also included in the present invention are methods to reduce IgG-mediated tissue damage. The method includes the step of administering to an animal a therapeutic composition of the present invention.

Another embodiment of the present invention is a therapeutic composition that is capable of stimulating an IgG humoral immune response in an animal. Yet another embodiment of the present invention is a therapeutic composition that improves the therapeutic affects of an antibody that is administered to an animal to treat, by [opsinization] opsonization or FcγR-dependent effector functions (e.g. antibody-dependent FcγR-mediated cytotoxicity, phagocytosis or release of cellular mediators), a particular disease, including, but not limited to, cancer or infectious disease (e.g. oral infections such as HIV, herpes, bacterial infections, yeast infections or parasite infections). Such a therapeutic composition includes one or more stimulatory compounds that have increased binding to IgG, enhance binding of IgG to FcγR, enhance dimer formation of an FcγR and/or enhance signal transduction through the FcγR. Also included in the present invention is a method to stimulate a humoral immune response. The method includes the step of administering to an animal a therapeutic composition of the present invention.--

Please amend the paragraph on page 56, lines 1-16, as follows:

--Another embodiment of the present invention is a therapeutic composition that is capable of stimulating a IgE humoral immune response in an animal. Yet another embodiment of the present

invention is a therapeutic composition that improves the therapeutic affects of an antibody that is administered to an animal to treat, by [opsinization] opsonization or FcεR-dependent effector functions (e.g. phagocytosis or release of cellular mediators), a particular disease. Such a therapeutic composition includes one or more stimulatory compounds that have increased binding to IgE, enhance binding of IgE to FcεRI, enhance dimer formation of FcεRI and/or otherwise enhance signal transduction through the FcεRI. Also included in the present invention is a method to stimulate a humoral immune response. The method includes the step of administering to an animal a therapeutic composition of the present invention.--

Please amend the paragraph bridging page 69, line 22 to page 70, line 4, as follows:

--A therapeutic composition of the present invention can comprise one or more therapeutic compounds of the present invention. A therapeutic composition can further comprise other compounds capable of reducing Ig-mediated responses or increasing a humoral immune response. For example, a therapeutic composition of the present invention useful for reducing tissue damage can also include compounds that block recruitment of inflammatory cells, such as by, for example, blocking complement fixation, extravasation, block binding of viral proteins to FcR, block [opsinization] opsonization or enhance normal and passive antibody immunity. A therapeutic composition of the present invention useful for reducing Ig-mediated inflammation can include compounds that block recruitment of inflammatory cells and/or block signal transduction pathway which leads to the release of inflammatory mediators.--